Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (withdrawn) A method of treating, preventing or ameliorating a disease responsive to induction of the caspase cascade in an animal, comprising administering to said animal a compound which binds specifically to an Apoptosis Inducing Protein (AIP), wherein said compound induces activation of the caspase cascade in said animal and said disease is treated, prevented or ameliorated;
with the proviso that said compound is not gambogic acid (GA) or a GA-related compound.

2. (withdrawn) The method of claim 1, wherein said AIP is a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP).

3. (withdrawn) The method of claim 1, wherein said AIP is a Clathrin Heavy Chain Related Apoptosis Inducing Protein (CHCRAIP).

4. (withdrawn) The method of claim 1, wherein said AIP is an IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein (IQGAPRAIP).

5. (withdrawn) The method of claim 1, wherein said AIP is a Heat Shock Protein Related Apoptosis Inducing Protein (HSPRAIP).

6. (withdrawn) The method of claim 2, wherein said disease is a hyperproliferative disease.

7. (withdrawn) The method of claim 6, wherein said disease is cancer.

8. (withdrawn) The method of claim 7, wherein said cancer is Hodgkin's disease, non-Hodgkin's lymphomas, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinomas, ovarian carcinomas, lung carcinomas, Wilms' tumor, cervical carcinomas, testicular carcinomas, soft-tissue sarcomas, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinomas, chronic granulocytic leukemia, primary brain carcinomas, malignant melanoma, small-cell lung carcinomas, stomach carcinomas, colon carcinomas, malignant pancreatic insulinoma, malignant carcinoid carcinomas, malignant melanomas, choriocarcinomas, mycosis fungoides, head and neck carcinomas, osteogenic sarcoma, pancreatic carcinomas, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinomas, thyroid carcinomas, esophageal carcinomas, malignant hypercalcemia, cervical hyperplasia, renal cell carcinomas, endometrial carcinomas, polycythemia vera, essential thrombocytosis, adrenal cortex carcinomas, skin cancer, or prostatic carcinomas.

9. (withdrawn) The method of claim 2, wherein said disease is an inflammatory disease.

10. (withdrawn) The method of claim 2, wherein said compound is identified by determining whether said compound binds specifically to a TRRAIP.

11. (withdrawn) The method of claim 10, wherein said TRRAIP is a transferrin receptor protein.

12. (withdrawn) The method of claim 2, wherein said compound induces apoptosis in the cells of said animal within 15 minutes to 10 hours, thereby treating, preventing or ameliorating said disease.

13. (withdrawn) The method of claim 2, wherein the molecular weight of said compound is between 250 to 20,000 Daltons.

14. (currently amended) A method of identifying potentially therapeutic anticancer compounds comprising:

(a) contacting a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP) ~~encoded by~~ having the amino acid sequence of SEQ ID NOS:1, 2, 3 or 8 and a detectably labeled gambogic acid (GA) or GA-related compound with one or more test compounds; and

(b) monitoring whether said one or more test compounds displaces said GA or GA-related compound and binds to said TRRAIP

wherein compounds which bind said TRRAIP are potentially therapeutic anticancer compounds.

15. (cancelled)

16. (withdrawn) The method of claim 14, wherein said AIP is a Clathrin Heavy Chain Related Apoptosis Inducing Protein (CHCRAIP).

17. (withdrawn) The method of claim 14, wherein said AIP is an IQ motif containing GTPase Activating Protein Related Apoptosis Inducing Protein (IQGAPRAIP).

18. (withdrawn) The method of claim 14, wherein said AIP is a Heat Shock Protein Related Apoptosis Inducing Protein (HSPRAIP).

19. (cancelled)

20. (previously presented) The method of claim 14, wherein said monitoring of (b) comprises determining whether said one or more test compounds bind to said TRRAIP in a competitive or noncompetitive homogeneous assay.

21. (original) The method of claim 20, wherein said homogeneous assay is a fluorescence polarization assay or a radioassay.

22. (previously presented) The method of claim 14, wherein said monitoring of (b) comprises determining whether said one or more test compounds bind to said TRRAIP in a competitive heterogeneous assay.

23. (original) The method of claim 22, wherein said heterogeneous assay is a fluorescence polarization assay or a radioassay.

24. (previously presented) The method of claim 14, wherein said TRRAIP comprises a detectable label.

25. (original) The method of claim 24, wherein said detectable label is selected from the group consisting of a fluorescent label and a radiolabel.

26. (previously presented) The method of claim 20, wherein said assay is a competitive assay comprising gambogic acid having a detectable label or a gambogic acid-related compound having a detectable label wherein in (b) said label is detected.

27. (original) The method of claim 26, wherein said detectable label is selected from the group consisting of a fluorescent label and a radiolabel.

28. (previously presented) The method of claim 22, wherein said competitive heterogenous assay comprises gambogic acid having a detectable label or a gambogic acid-related compound having a detectable label wherein in (b) said label is detected.

29. (original) The method of 28, wherein said detectable label is selected from the group consisting of a fluorescent label and a radiolabel.

30. (previously presented) The method of claim 14, wherein said TRRAIP is present in cells *in vitro*.

31. (previously presented) The method of claim 14, wherein said potentially therapeutic anticancer compound is selected from the group consisting of 1-allyl-1,3,3a,4,5,12a-hexahydro-7,13-dioxo-1,5-methano-furo[3,4-*d*]xanthene, 1-allyl-1,3,3a,4,4a,11a-hexahydro-10,12-dioxo-1,4a-methano-furo[3,4-*b*]xanthene, 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,5,12a-hexahydro-7,13-dioxo-1,5-methano-furo[3,4-d]xanthene, 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,4a,11a-hexahydro-10,12-dioxo-1,4a-methano-furo[3,4-b]xanthene, 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,5,10a-hexahydro-7,11-dioxo-9-phenyl-1,5-methano-furo[3,4-i]chromene, and 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,4a,9a-hexahydro-8,10-dioxo-6-phenyl-1,4a-methano-furo[3,4-g]chromene.

32. (withdrawn) A method of prognosing the efficacy of an anti-cancer AIP binding composition in a cancer patient comprising:

(a) taking a fluid or tissue sample from an individual manifesting a cancer;

(b) quantifying the total mRNA encoding the AIP which binds said anti-cancer AIP binding composition;

(c) calculating a ratio comprising the quantity of said mRNA to the average quantity of said mRNA in a fluid or tissue not manifesting said cancer;

wherein a ratio greater than 1 indicates that said anti-cancer AIP binding composition is efficacious.

33. (withdrawn) The method of claim 32, wherein said AIP is a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP).

34. (withdrawn) A method of prognosing the efficacy of an anti-cancer AIP binding composition in a cancer patient comprising:

(a) taking a fluid or tissue sample from an individual manifesting a cancer;

(b) quantifying in said sample the AIP which binds said anti-cancer AIP binding composition;

(c) calculating a ratio comprising the quantity of said AIP to the average quantity of said AIP in a fluid or tissue not manifesting said cancer;

wherein a ratio greater than 1 indicates that said anti-cancer AIP binding composition is efficacious.

35. (withdrawn) The method of claim 34, wherein said AIP is a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP).

36. (withdrawn) A complex, comprising:

i) an AIP; and

ii) an AIP binding compound;

with the proviso that said AIP binding compound is not GA or a GA-related compound.

37. (withdrawn) The complex of claim 36, wherein said AIP is a Transferrin Receptor Related Apoptosis Inducing Protein (TRRAIP).

38. (withdrawn) A compound selected from the group consisting of 1-allyl-1,3,3a,4,5,12a-hexahydro-7,13-dioxo-1,5-methano-furo[3,4-*d*]xanthene, 1-allyl-1,3,3a,4,4a,11a-hexahydro-10,12-dioxo-1,4a-methano-furo[3,4-*b*]xanthene, 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,5,12a-hexahydro-7,13-dioxo-1,5-methano-furo[3,4-d]xanthene, 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,4a,11a-hexahydro-10,12-dioxo-1,4a-methano-furo[3,4-b]xanthene, 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,5,10a-hexahydro-7,11-dioxo-9-phenyl-1,5-methano-furo[3,4-i]chromene, and 1-(3-methyl-2-butenyl)-3,3-dimethyl-1,3,3a,4,4a,9a-hexahydro-8,10-dioxo-6-phenyl-1,4a-methano-furo[3,4-g]chromene.

39. (withdrawn) A pharmaceutical composition comprising the compound of claim 38 and a pharmaceutically acceptable carrier.

40. (withdrawn) A method of identifying potentially therapeutic anticancer compounds comprising:

(a) contacting an antibody to gambogic acid (GA) or a GA-related compound; and

(b) determining whether said compound binds to said antibody;

wherein compounds which bind said antibody are potentially therapeutic anticancer compounds.

41. (withdrawn) A detectably labeled gambogic acid or gambogic acid related compound comprising

i) gambogic acid or a gambogic acid related compound;

ii) optionally a linker; and

iii) a label;

wherein said gambogic acid or said gambogic acid related compound is covalently linked to said label optionally via said linker.

42. (withdrawn) The composition of claim 41, wherein said linker is *N,N*-(1,2-aminoethyl); *N,N*-(2-{2-[2-(2-aminoethoxy)-ethoxy]-ethoxy}-aminoethyl); *N,N*-(2-[2-(2-aminoethoxy)-ethoxy]-aminoethyl); *N,N*-[2-(2-{2-[2-(2-aminoethoxy)-ethoxy] ethylcar-bamoyl}-ethyldisulfanyl)-aminoethyl]; *N,N*-(amidoacetamido); *N*-[(5-{2-[2-(2-aminoethoxy)-ethoxy]-ethylcarbamoyl}-pentyl)-carboxamide]; *N*-({5-[2-(2-aminoethyldisulfanyl)-ethylcarbamoyl]-pentyl})-carboxamide; *N,N*-[(5-aminopentyl)-thioureidyl]; or *N*-({2-[2-(2-aminoethoxy)-ethoxy]-ethyl}-carboxamide).

43. (withdrawn) The composition of claim 41, wherein said detectable label is biotin, a fluorescent label, or a radiolabel.

44. (withdrawn) A composition comprising

i) gambogic acid or a gambogic acid related compound;

ii) optionally a linker; and

iii) a solid phase;

wherein said gambogic acid or said gambogic acid related compound is covalently linked to said solid phase optionally via said linker.

45. (withdrawn) The composition of claim 44, wherein said solid phase is amino-agarose or *N*-hydroxysuccinimidylcarboxylagarose.

46. (withdrawn) A method of preparing the composition of claim 44, comprising bonding *N*-hydroxysuccinimidylgambogate to said solid phase.

47. (previously presented) The method of claim 14, further comprising contacting a cell with a TRRAIP binding test compound identified in (b) and monitoring apoptotic activity.